High-efficiency stem cell fusion-mediated assay reveals Sall4 as an enhancer of reprogramming.

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Public Summary:

Scientific Abstract:
Several methods allow reprogramming of differentiated somatic cells to embryonic stem cell-like cells. However, the process of reprogramming remains inefficient and the underlying molecular mechanisms are poorly understood. Here, we report the optimization of somatic cell fusion with embryonic stem cells in order to provide an efficient, quantitative assay to screen for factors that facilitate reprogramming. Following optimization, we achieved a reprogramming efficiency 15-590 fold higher than previous protocols. This allowed observation of cellular events during the reprogramming process. Moreover, we demonstrate that overexpression of the Spalt transcription factor, Sall4, which was previously identified as a regulator of embryonic stem cell pluripotency and early mouse development, can enhance reprogramming. The reprogramming activity of Sall4 is independent of an N-terminal domain implicated in recruiting the nucleosome remodeling and deacetylase corepressor complex, a global transcriptional repressor. These results indicate that improvements in reprogramming assays, including fusion assays, may allow the systematic identification and molecular characterization of enhancers of somatic cell reprogramming.